

Research Digest

Oral contraceptive use associated with myocardial infarction and ischemic stroke but not angina

Question

Is the risk of cardiovascular disease increased in women who take oral contraceptives?

Design

Cohort study with up to 26 years of follow-up.

Setting

Seventeen family planning clinics in England and Scotland.

Participants

A total of 17,032 women who attended a family planning clinic between 1968 and 1974 were included in the study. Women were included if they were married, white, had British citizenship, and were between 25 and 39 years old. Participants were sent annual questionnaires that requested information on their method of contraception, past medical history, social history, and height and weight. Altogether, 15,292 women (90%) were still participating at age 45, at which time they were sent a questionnaire that also requested information on smoking status.

Assessment of risk factors

At age 45, women were categorized as never-users of oral contraceptives (OCs) (n=5881), users of OCs for >8 years (n=3520), or users for ≤8 years (n=5891).

Main outcome measures

Myocardial infarction (MI), angina, ischemic stroke, subarachnoid hemorrhage, intracerebral hemorrhage, and transient ischemic attack. The rates were adjusted for age, social class, smoking, and obesity (all diagnoses) and for parity (MI and angina). A restricted analysis was done, excluding women with hypertension, diabetes, or hyperlipidemia.

Main results

No association between the use of oral contraceptives and myocardial infarction was seen in the whole study population. When women with hypertension, hyperlipidemia, or diabetes were excluded (restricted analysis), an increased risk of MI existed among women who used OCs for up to 8 years (relative risk [RR] 1.9, 95% confidence interval [CI] 1.0-3.5). In further analyses, this risk was seen only in heavy smokers (≥15 cigarettes/day). In heavy smokers, the RR for MI in ever-users of OCs was 4.2 (95% CI 1.4-16.6), or for every 1060 heavy smokers taking OCs, one additional MI occurred per year. The risk

of angina was generally similar in OC users and never-users. The risk of ischemic stroke was increased in current users. After adjustment for age, social class, smoking, and obesity, the RR was 2.4 (95% CI 1.1-5.1); the adjusted RR after restriction was 2.9 (95% CI 1.3-6.7), or 1 additional stroke per year for every 5880 OC users.

Conclusion

Oral contraceptive use was associated with an increased risk of myocardial infarction in heavy smokers. Current use was associated with a small increase in the risk of ischemic stroke.

COMMENTARY

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Stroke and myocardial infarction are rare events among women of reproductive age. Prospective examination of the effects of oral contraceptives on these outcomes requires large cohorts and long follow-up times. Women already known to be at risk of stroke or myocardial infarction are unlikely to be prescribed oral contraceptives, which makes it difficult to define their effects on women with risk factors for cardiovascular disease. Because the estrogen dose in oral contraceptives has progressively decreased over the past 30 years, it is even more complicated to apply results from older studies to women using the current oral contraceptives.

This study is one of several recent reports revisiting the cardiovascular effects of oral contraceptives.¹⁻⁴ This study, with more than 20 years of follow-up and over 300,000 woman-years of observation, is well-suited for rare events. It is not much help with understanding the effects of current low-dose estrogen oral contraceptives because 68% of the woman-years of exposure are from oral contraceptives containing 50 µg of estrogen. It can, however, serve with other reports to establish a benchmark for the worst cardiovascular effects of oral contraceptives in healthy women. Another recent study suggests that lower-dose oral contraceptives may not increase the risk of myocardial infarction, even among smokers,³ although women who use low-dose oral contraceptives and who smoke are at an increased risk of stroke.⁴

For nonsmokers with normal blood pressure, the risk of myocardial infarction is not affected by oral contraceptive use. An increased risk of myocardial infarction is confined to women smoking ≥15 cigarettes per day.

In contrast, the health risks of smoking are enormous. Clinicians need to help patients quit smoking and to work together for public health regulations that make it harder for young people to start.

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- 3 Sidney S, Siscovick DS, Petitti DB, et al. Myocardial infarction and use of low-dose oral contraceptives: a pooled analysis of 2 US studies. *Circulation* 1998;98:1058-1063.
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